REMARKS

I. Introduction

Receipt is acknowledged of a non-final Office Action dated February 25, 2004. In the action the Examiner rejected claims 3-10, 12, 13, 60 and 61 as allegedly not enabled and for failing to meet the written description requirement. The Examiner also objected to the specification for formality reasons.

II. Status of the Claims

In this response applicants amended claims 3-5, 12 and 13. Support for new claim 62 can be found in originally filed claim 1 and in the specification on page 20. Support for new claim 63 can be found in originally filed claim 5, and new claims 64-66 can be found in the specification on page 6, last full paragraph. Upon entry of this amendment, claims 3-10, 12, 13, 60-66 will be under examination.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

III. Objections to the Specification

The specification was objected to for allegedly referring only to Figure 1 as showing the coding region of both PANEC-1 and 2. Applicants corrected the instant specification on page 15, last paragraph. Therefore, Applicants respectfully request reconsideration and withdrawal of the objection.

IV. Rejection of the Claims Under 35 U.S.C. § 112, first paragraph

A. New Matter Rejection

Claims 3-10, 12, 13, 60 and 61 were rejected under 35 U.S.C. § 112 for allegedly containing subject matter which was not described in the instant specification. Office Action at 6. In particular, the Examiner stated that "the new limitations of 'has an insertion of deletion of 1-5 amino acids compared with SEQ ID NO: 4' and 'has one or more amino acid

substitutions as compared with SEQ ID NO: 4 and has the amino acid sequence of SEQ ID NO: 4 at amino acids...' appear to represent new matter." Office Action at 6.

In the interest of expediting prosecution, applicants amended claim 12 to recite a polypeptide variant that has chemokine activity and comprises at least 90% sequence identity, instead of a deletion or substitution of a specific amino acid identified by position numbers. Support for this amendment can be found in originally filed claim 1 and on page 20 of the present specification. Applicants respectfully request reconsideration and withdrawal of the rejection.

B. Written Description Rejection

Claims 3, 6-9, 12, 13, 60 and 61 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to meet the written description requirement. Specifically, the Examiner stated that "there is no record or description which would demonstrate conception of any nucleic acids encoding proteins modified by addition, insertion, deletion, substitution or inversion with the disclosed SEQ ID No: 4 therefore possessing one or more amino acid differences such that a different amino acid sequence is encoded which retains same function as SEQ ID NO:4, which function is not clearly set forth in the specification." Office Action at 20-21. The examiner, however, conceded that the specification describes nucleic acids encoding SEQ ID NO: 4, a nucleic acid comprising SEQ ID NO: 3, fragments of SEQ ID NO: 3, and polynucleotides that encode amino acid sequences consisting of SEQ ID NO: 4. Applicants respectfully request reconsideration and withdrawal of the rejection.

1. The specification adequately describes polynucleotides encoding a polypeptide having chemokine activity and sharing at least 90% sequence identity to SEQ ID NO:4

In the interest of expediting prosecution, applicants amended the claims to recite a polypeptide variant that "shares at least 90% sequence identity to SEQ ID NO: 4." Also, as stated in the claim, the claimed polynucleotide encodes a polypeptide that has chemokine activity.

Because of the redundancy in the genetic code and the teachings in the instant application, a skilled artisan would know what nucleotides to change in order to encode the same corresponding amino acid in SEQ ID NO: 4, as well as which amino acids can be changed so as to produce a functionally equivalent protein. See, for example, specification at 6 and 8. Functionality of the protein can then be determined based on known methods. Indeed, the polypeptide that is at least 90% identical to SEQ ID NO: 4 must have chemokine activity. Chemokines are defined in the art and a skilled artisan would know what properties are associated with chemokines, and chemokines in the C-C family, and how to assess chemokine activity. Thus, based on the teachings of the specification, a skilled artisan would readily be able to measure the activity of the polypeptide variants by following the assay described in example XII. See specification at 21.

The Examiner also indicated that "the specification does not discuss which fragments of SEQ ID NO: 4 are essential for the maintenance of 'chemokine activity.'" Applicants respectfully assert that a skilled artisan, based on the teachings of the specification, could readily make a polypeptide variant that share 90% sequence identity to SEQ ID NO: 4 and assess chemokine activity of the resulting polypeptide by methods known in the art, as well as by methods described in the instant specification (e.g., example XII).

2. The specification adequately describes polynucleotides that encode polypeptides with chemokine activity

Applicants respectfully assert that the specification describes the claimed polynucleotides as encoding chemokines that are members of the C-C family. The specification further goes on to describe that the polynucleotides of the present invention encode PANEC-1 and 2, specifically, which can be used in methods for treating inflammation and disease of the pancreas. Specification at 12.

The function of chemokines is well known in the art, and is also explained in the instant specification. See specification at 3. Indeed, the Examiner even pointed to the cited art (e.g., Caput et al) and asserted that this reference teaches a polypeptide variant of SEQ ID NO: 4, "wherein the variant has chemokine activity." Office Action at 23. Thus, based on

the teachings in the present specification and information known in the art, a skilled artisan would understand what is meant by "chemokine activity."

Additionally, the structural features of the various chemokines in the C-C and CXC families is described. Therefore, applicants respectfully assert that the Examiner 's assertion that the "function [of SEQ ID NO: 4] is not clearly set forth in the specification" is incorrect.

3. The application describes polynucleotides encoding polypeptide fragments of SEQ ID NO: 4 that are immunogenic or biologically active

Likewise, polynucleotides that encode an immunogenic or biologically active fragment of SEQ ID NO: 4 are also described in the present application. Foremost, one of skill in the art would know what is meant by an immunogenic or biologically active fragment and would know how to assess the "immunogenic" or "biologically active" functionality as recited in the claims. In addition to prior art methods, the specification describes methods for preparing fragments of SEQ ID NO: 4 that are immunogenic. See specification at 19.

The specification also describes an assay for assessing PANEC activity and this assay can be used to test the biological activity of the presently claimed fragments of SEQ ID NO: 4. See specification at 21, example XII. Likewise, the chemotactic and non-chemotactic cell activation activity of PANEC can be assayed by known methods.

4. The specification describes how to identify polynucleotides that are naturally occurring

Additionally, the specification describes naturally occurring polynucleotides. See, for example, the present application discloses that naturally occurring PANEC "refers to PANECs produced by human cells that have not been genetically engineered and specifically contemplates various PANECs arising from post-translational modifications of the polypeptide." Specification at 6. As such, a skilled artisan would know how to identify naturally occurring polynucleotides as recited in the claim. Nevertheless, in the interest of expediting prosecution, applicants deleted the phrase "naturally occurring" from claim 12.

For at least these reasons, Applicants' claims satisfy the written description requirement of § 112, first paragraph, and therefore, withdrawal of this ground for rejection is respectfully requested.

V. Rejection of the Claims Under 35 U.S.C. § 112, second paragraph

Claims 3-10, 12, 13, 60 and 61 were rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. In particular, the Examiner stated that the phrases "allelic or recombinant variant" and "polynucleotide variant of SEQ ID NO: 3" are unclear, and that the last line in claim 12 is labeled incorrectly. Office Action at 21. Applicants respectfully request reconsideration and withdrawal of the rejection.

Applicants respectfully assert that it is clear what is meant by the phrase "allelic or recombinant variant." For example, the specification describes that a recombinant variant as a polypeptide that differs from a naturally occurring PANEC. Specification at 6. In addition, the specification describes that the term "recombinant" may also refer to a polynucleotide encoding PANEC-1 and PANEC-2, and includes allelic or recombinant polynucleotide variants. Specification at 7. But in the interest of expediting prosecution, claim 3 is not directed to a polynucleotide encoding "an allelic or recombinant variant" but instead recites "a polynucleotide encoding a polypeptide variant of the amino acid of SEQ ID NO: 4."

Applicants also changed the numbering of the claim elements in pending claim 12. Applicants trust that these amendments address the examiner's concerns.

VI. Rejection of the Claims Under 35 U.S.C. § 101

Claims 3-10, 12, 13, 60 and 61 were rejected under 35 U.S.C. § 101 as allegedly lacking utility. Specifically, the Examiner stated that "[w]hile [the] asserted utility is specific, it is not substantial...because further experimentation would be required to reasonably confirm that in fact a real world utility exists wherein these molecules can be used in diagnostics." Office Action at 11-12. Applicants respectfully disagree and request reconsideration and withdrawal of the rejection..

A. The specification describes a "real world" use for the claimed polynucleotides

The M.P.E.P. provides guidelines for the Office in examining applications for utility and in fact recites that "[p]ractical considerations require the Office to rely on the inventor's understanding of his or her invention in determining whether and in what regard an invention is believed to be 'useful.'" The PTO's own guidelines continue to say that "[b]ecause of this, Office personal should focus on and be receptive to assertions made by the applicant that an invention is 'useful' for a particular reason." M.P.E.P. § 2107.01 (I). Indeed, the instant specification provides that the claimed polynucleotides of the present invention encode polypeptides that are members of the C-C chemokine family and "are useful in diagnostic assays based on chemokine production in cases of inflammation or disease affecting the pancreas." Specification at 8.

The specification further describes the encoded PANEC chemokines as suitable for making antibodies that bind PANEC-1 or PANEC-2. The PANEC specific antibodies can then be used "as bioactive agents to treat inflammation or disease of the pancreas including...hereditary diseases affecting pancreatitis; biliary disease; [and] infiltrative diseases such as leukemias and lymphomas." Specification at 12. Thus, the examiner's assertion that the specification does not describe a specific and substantial utility for the claimed invention is unfounded.

Furthermore, the specification provides that PANEC, which is encoded by the claimed polynucleotides, can lead to activation of cells such as monocytes, macrophages and T-lymphocytes which can lead to tissue damage or destruction and assays detecting conditions caused or exacerbated by overexpression of PANEC allows for an accelerated diagnosis and proper treatment. Specification at 8. This is in fact a substantial utility for the claimed PANEC chemokines. Indeed, the M.P.E.P. provides that "[a]n assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a 'real world' context of use in identifying potential candidates for preventive measures and further monitoring." M.P.E.P. § 2107. Thus, the Examiner 's assertion that the specification lacks substantial utility is not supported.

The Examiner further states that "the language in the specification appears to be prophetic" and that the claimed polypeptides of the present invention "may activate any one of these [previously disclosed cell types] or some other undisclosed molecule, but it is equally suggestive that it may not activate any one of these." Office Action at 13-14. However, applicants respectfully assert that the Examiner 's requirement for disclosure of the mechanism/target cell population by which the PANEC polypeptides act is not tenable. Applicants have described that the claimed PANEC polypeptides are chemokines, that they are members of the C-C chemokine family, and that they can be used in diagnostic assays and methods for treating inflammation or disease of the pancreas. The burden is on the applicants to show specific and substantial utility for the invention and applicants respectfully assert that they have met that burden. To support specific and substantial utility, applicants are not required to disclose a mechanism of action or target cell for the PANEC polypeptides.

VII. Rejection of the Claims Under 35 U.S.C. § 102

Claims 3, 6-9, 12, 13, 60 and 61 were rejected under 35 U.S.C. § 102 as allegedly anticipated by Caput et al., PCT Publication WO 92/09629. In the action, the Examiner stated that the claims of the present invention "encompass any isolated nucleic acid encoding a polypeptide that is a variant of SEQ ID NO: 4[,] wherein said variant has an insertion or deletion of 1-5 amino acids relative to SEQ ID NO: 4, but can have any number of such insertions or deletions." Office Action at 23. Applicants respectfully request reconsideration and withdrawal of the rejection.

Applicants respectfully assert that Caput does not teach a polynucleotide of SEQ ID NO: 3, or a polynucleotide encoding a polypeptide of SEQ ID NO: 4. Caput also does not teach a polynucleotide that encodes a polypeptide that consists essentially of about 1 to 5 amino acid insertions or deletions compared with SEQ ID NO. 4 and shares at least 90% sequence identity with SEQ ID NO: 4. Indeed, the Examiner stated that the nucleic acid taught by Caput "contains a large number of additional insertions and deletions relative to SEQ ID NO:4." Office Action at 23.

The Examiner also stated that Caput teaches "a polynucleotide that encodes residues 75-78 of SEQ ID NO: 4, and this four amino acid fragment would be immunologically active, that is able to raise an antibody." Office Action at 24. Without acquiescing to the Examiner's rejection, applicants amended claim 3 to recite that an immunogenic fragment of a polypeptide consisting essentially of SEQ ID NO: 4 also possesses biological activity. Support for this amendment can be found on page 7, first full paragraph of the present specification.

VIII. Claim Objections

All pending claims were objected because of incorrect numbering of base claim 1 (dependent claims 3-10) and base claim 12 (dependent claims 12, 13, 60 and 61). Applicants amended the claims to further clarify the present invention. Accordingly, the present rejection is moot.

IX. Sequence Listing

The Examiner asserts that there are two amino acid sequences recited in figures 3A-3C that are not identified by proper SEQ ID NO in the amended description of the drawings. Applicants have amended the description of figures 3A-3C on page 5, line 20, to recite that 226152 = SEQ ID NO: 2 and 223187 = SEQ ID NO: 4. *See,* page 5. Applicants respectfully request withdrawal of the objection.

The Examiner further asserts that the CRF transferred from the parent application and the paper copy of the sequence listing filed 10/25/01 are not identical. Please substitute the CRF copy of the Sequence Listing and the Sequence Listing filed concurrently herewith for the CRF copy of the Sequence Listing and the Sequence Listing previously filed. Please insert the substitute copy of the Sequence Listing filed herewith following the specification and before the claims, and renumber pages 27-35 of the Sequence Listing as pages 47-55.

In view of the foregoing arguments, it is respectfully requested that the present rejections be withdrawn.

CONCLUSION

Reconsideration of the present application in view of the foregoing amendments and arguments is kindly requested.

It is respectfully urged that the present application is now in condition for allowance. Early notice to that effect is earnestly solicited.

Examiner Switzer is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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